CMA Ethylene Glycol Panel Discussion on the Study

"Exposure to glycols and their renal effects in motor servicing workers"
by J. Laitinen, J. Liesivuori, and H. Savolainen

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Abstract: *Ten car mechanics frequently exposed to glycol-based cooling liquids were following during a workshift. Airborne ethylene and propylene glycol concentrations in the car mechanics' environment were measured. The car mechanics gave urine samples after the workshift and their excretion of ethylene glycol, propylene glycol, oxalic acid, calcium and ammonia was analysed and compared to that of unexposed office workers. Urinary succinate dehydrogenase activity and glycosamionglycans were also measured in both groups. Airborne ethylene and propylene glycol concentrations in the car mechanics' environment were negligible. Urinary ethylene glycol excretion in exposed workers was significantly higher than that in unexposed workers, but propylene glycol excretion was at the same levels as in controls. In the exposed groups, the excretion of the end metabolite of ethylene glycol, oxalic acid (47 ± 11 mmol/mol creatinine, mean ± SD. n = 10) differed slightly from that of controls (36 ± 14 mmol/mol creatinine, mean ± SD. n = 10). Urinary excretion of ammonia was higher among exposed workers than office workers. The excretion of calcium did not differ from that of controls. A marginally decreased urinary succinate dehydrogenase activity was found in the exposed men. The excretion of glycosaminoglycans was significantly lower in exposed workers. Therefore, it seems that ethylene glycol is absorbed by skin contact. The internal body burden is associated with oxaluria and increased ammonigenesis typical of chronic acidosis.*

Panel comments:

TITLE AND ABSTRACT MISREADING IN NOTING RENAL EFFECTS

It should be duly noted that although both the title and study abstract indicate that renal effects were seen in the mechanics as a result of their exposure to glycols, this is not the case. In fact, workers were found to be in "habitual good health" and no toxic effects were noted for either group. Moreover, biochemical findings are not unexpected in car mechanics involved in heavy engine repairs.

QUESTIONABLE RESULTS FOUND IN CONTROL SAMPLES

The similar high background value in control urine for both propylene glycol and ethylene glycol (2.3 and 1.7 mmol/mol creatinine, respectively) is perplexing. It seems unrealistic to expect ethylene glycol and propylene glycol to be present in control urine at similar levels. The authors suggest that the propylene glycol levels could be due to its use in pharmaceutical products, which the workers may have taken. If this were the case, however, why is ethylene glycol similarly high in the controls? Also, why is the standard deviation of control propylene glycol values so small (2.3 ± 1.4)? If these higher levels of propylene glycol were truly due to pharmaceutical use, one would expect the values to have a much broader range – unless every one of the ten control subjects were taking the same amount of propylene glycol-containing pharmaceuticals.

QUESTIONABLE CLINICAL CHEMISTRY TECHNIQUES

It is unclear why the urine samples were not stored on ice, as is typically the case in biochemical research. In fact, the levels of ammonia seen in the samples is likely attributable to the improper sample storage.

[1] as published in Occupational Medicine, Vol 45, No. 5, 1995.

QUESTIONABLE ANALYTICAL METHODOLOGY USED

The method used for quantification of ethylene and propylene glycol in the urine ("Analytical Procedure for the Determination of 1,2 Propylene Glycol and Diethylene Glycol in Blood and Urine," Goen, T.H.) is unpublished, has not been validated in the peer-reviewed literature, and may be unreliable. In addition, the cited procedure indicates detection limits for ethylene glycol in urine at 2.0 mg/l. However, given the calculations below, the amount of EG for the workers was 1.32 - 2.52 mg/urine sample. Assuming that the urine sample was less than one liter, then these measurements were below the cited detection limit for the procedure used. Moreover, the amount of EG measured in the control subjects was only 0.31 - 0.62 mg/sample, well below the limit.

- Assuming the typical range of creatinine is 1000 - 1900 mg/24 hour urine, an 8-hour work shift would show 333 - 633 mg. With a GMW of 113, this equals a range of 2.95 - 5.6 mmol creatinine/8-hour shift, or 0.003 - 0.006 mol creatinine/8hour shift.
- Given the reported ratio of 7.3 mmol EG/mol creatinine in the workers, this results in 0.022 - 0.042 mmol of ethylene glycol or 1.32 - 2.52 mg of ethylene glycol in the urine samples (GMW = 60).
- Given the reported ratio of 1.7 mmol EG/mol creatinine in the control subjects, this results in 0.306 - 0.612 mg of ethylene glycol in the urine samples.

In addition, the analytical methods did not appear to be tested on interference's from other workplace solvents.

Speculations of cause and effect for non-statistically significant observations in urine analysis are very questionable.

RESULTS OF STUDY STILL DEMONSTRATE SMALL AMOUNT OF ETHYLENE GLYCOL ABSORBED

Because there was no ethylene glycol detected in the workers' breathing zones, the Laitinen study concludes the significant levels of ethylene glycol found in the workers' urine are due to absorption through skin contact. However, there is no direct evidence to support this finding. Moreover, due to concerns with methodology (see discussion below), the study results and conclusions remain questionable. Nonetheless, if the increase in ethylene glycol excretion was due to skin contact, the total amount absorbed through the skin was actually quite low -- about 2.0 mg, and could likely be metabolized by the body without causing the implied renal effects. In fact, the calculated reference dose for ethylene glycol is 2.0 mg/kg/day, which equates to 140 mg per day for an average adult.

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